

Serial No.: 10/601,311  
 Filing Date: June 20, 2003

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REMARKS

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Reconsideration is respectfully requested. Claims 1, 4, 9, 12, 15, 18, and 22-36 are pending. Claims 2, 3, 5-8, 10, 11, 13, 14, 16, 17, and 19-21 have been canceled. Claims 29, 31, 32, 33, 35 and 36 have been amended. Claims 18, 22-28, 30, and 34 have been withdrawn. No new matter has been added as a result of the amendments. Amendment to and cancellation of the claims does not affect inventorship.

Applicants thank the Examiner for the allowance of claims 1, 4, 9, 12 and 15. Claims 29, 31-33, 35 and 36 stand rejected.

Applicants have not dedicated or abandoned any unclaimed subject matter and moreover have not acquiesced to any rejections made by the Patent Office. Applicants reserve the right to pursue prosecution of any presently excluded claim embodiments in future continuation and/or divisional applications.

Claim Amendments

Claims 29, 31-33, and 35-36 have been amended. Support is found in the specification, for example, at paragraphs [00192] to [00198].

Claim Rejection Under 35 U.S.C. § 112

Written Description

Claims 29, 32-33 and 35-36 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. The Examiner states that:

The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The courts have described the essential question to be addressed in a description requirement issue in a variety of ways. An objective standard for determining compliance with the written description requirement is, "does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed." *In re Gosteli*, 872 F.2d 1008, 1012 (Fed. Cir. 1989). Under *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64 (Fed. Cir. 1991), to satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date

Serial No.: 10/601,311  
Filing Date: June 20, 2003

sought, he or she was in possession of the invention, and that the invention, in that context, is whatever is now claimed. The test for sufficiency of support in a parent application is whether the disclosure of the application relied upon "reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter." *Ralston Purina Co. v. Far-Mar-Co., Inc.*, 772 F.2d 1570, 1575 (Fed. Cir. 1985) (quoting *In re Kaslow*, 707 F.2d 1366, 1375 (Fed. Cir. 1983)). The subject matter of the claim need not be described literally (i.e., using the same terms or *in haec verba*) in order for the disclosure to satisfy the description requirement. See M.P.E.P. § 2163.02 (emphasis added).

The Examiner appears to be taking the position that the term "non-crystalline" introduced into claims 29, and 31-33 by amendment constitutes "new matter" because the term does not appear anywhere in the specification. As the M.P.E.P clearly states, the claims need not use the exact same terms as used in the specification in order to satisfy the written description requirement. See M.P.E.P. § 2163.02. Additionally, the specification conveys the subject matter encompassed in the rejected claims. For example, claim 29 is directed to a non-crystalline protein consisting of SEQ ID NO:4, which represents amino acid residues 227-556 of AKT3. SEQ ID NO:4 is described in Figure 1, which forms an integral of the application's specification. Additionally, the specification, see paragraphs [00192] to [00194] for example, teaches that in order to obtain a crystalline form of a protein, it is first necessary to express the protein in a soluble i.e, non-crystalline form following which, the soluble form of the protein is subjected to crystallization under appropriate conditions. It is unclear to Applicant what Examiner's issue really is. Since the specification clearly teaches the making of a soluble (non-crystalline) form of a protein, which in turn is crystallized to form a crystalline form of the protein, both crystalline and non-crystalline forms of the protein are taught. As such, the specification provides an adequate description of both forms of the protein, and thus claims to both crystalline and non-crystalline forms are fully supported.

For the same reasons set forth above, the subject matter of claim 33 which is directed to an "isolated non-crystalline" protein consisting of SEQ ID NO:4 is supported by the specification, for example paragraphs [00192] to [00194], which teaches the expression and isolation/purification of a protein encoded by a portion of the AKT3 gene.

Similarly, claims 31 and 32 which are directed to a "non-crystalline" and an "isolated non-crystalline" protein consisting of residues 136-461 of SEQ ID NO:1 is supported by the specification, paragraphs [00192] to [00194] and Figure 1 (SEQ ID NO:1, SEQ ID NO:3 and SEQ ID NO:4). The referenced paragraphs teach the cloning of a portion of a gene encoding residues 136-461, expression of

Serial No.: 10/601,311  
 Filing Date: June 20, 2003

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the cloned protein, and purification/isolation of the expressed protein. Furthermore, SEQ ID NO:1, SEQ ID NO:3 and SEQ ID NO: 4 provide descriptions of protein sequences that comprise residues 136-461, which can be prepared in non-crystalline form and isolated, based on the teachings of the specification at [00192] to [00194].

Regarding claims 35 and 36, the specification teaches SEQ ID NO:1, SEQ ID NO:3 and SEQ ID NO:4 that comprise residues 136-461, which can be crystallized based on the teachings of the specification at [00195] to [00198].

In sum, the specification provides sufficient description to convey to one of skill in the art that Applicants were in possession of the subject matter of claims 29, 31, 32, 33, 35 and 36 at the time of filing of the instant application. As such, the rejection based on lack of written description is improper and should be withdrawn.

#### Enablement

Claims 29, 31, 35 and 36 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement. The Examiner states:

Enablement requires a disclosure sufficient to allow a person of skill in the art to practice the full scope of the claimed invention without undue experimentation.

The standard for determining whether the specification meets the enablement requirement was cast in the Supreme Court decision of *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916) which postured the question: is the experimentation needed to practice the invention undue or unreasonable? That standard is still the one to be applied. *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988). The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. *In re Angstadt*, 537 F.2d 498,

With respect to claim 29 that is directed to a non-crystalline protein consisting of SEQ ID NO:4, Applicants have provided a detailed methodology of the process for isolating a non-crystalline form of SEQ ID NO:4 in paragraphs [00192] to [00194]. The scope of the claims is directed to a non-crystalline protein consisting of SEQ ID NO:4. Notwithstanding Applicant's disclosure, the methodologies of cloning and expression of proteins was very well known at the time the instant application was filed. Indeed, comparable to the scenario in *In re Wands*, there is considerable direction and guidance in the

Serial No.: 10/601,311  
Filing Date: June 20, 2003

specification, and a high level of skill in the art at the time the application was filed, for one of ordinary skill to practice the claimed invention set forth in claim 29 (i.e., non-crystalline protein consisting of SEQ ID NO:4) without undue experimentation.

Regarding claim 31, paragraph [00193] of the Specification teaches the cloning and expression of a soluble (non-crystalline) form of a protein comprising residues 136-461 of SEQ ID NO:1.

Regarding claims 35 and 36, contrary to the Examiner's assertions, Applicants have not claimed any crystal of the protein of SEQ ID NO:4 or a crystal containing residues 136-461 of SEQ ID NO:1, but rather have claimed crystals having specific space group and unit cell dimensions. With respect to claim 35 and 36, SEQ ID NO:1, SEQ ID NO:3 and SEQ ID NO: 4 provide descriptions of protein sequences that comprise residues 114-331, while paragraphs [00192] to [00198] teach the methodology of crystallization of a protein.

The Examiner states that "protein crystallization is a major hurdle in protein structure determination" and "protein crystallization is the major hurdle in protein structure determination". While that may have been true in years past, protein crystallization is presently a highly researched area of structural biology, a fact acknowledged by the Examiner himself. The Examiner states that "one skilled in the art would require additional guidance, such as information regarding the exact crystallization conditions for a protein consisting of residues 136-461." Applicants have provided a working example for the crystallization of SEQ ID NO:4 which comprises residues 136-461. Based on the level of knowledge available at the time the application was filed in 2003 (see reference list below), coupled with Applicant's disclosure, a skilled artisan would be able to make the necessary adjustments to the experimental conditions to arrive at the appropriate crystallization conditions for a protein comprising residues 136-461 of SEQ ID NO:1.

A simple search on Google Scholar for references relating to protein crystallization methods yielded in excess of 30,000 hits most of which had a publication date prior to 2003. A sampling of the references is provided below. Therefore, it is quite clear that the level of skill in the art was high, with respect to crystallization methods, at the time the application was filed. Hence, a skilled artisan would have been more than capable of arriving at the conditions for crystallization of a protein comprising residues 136-461 of SEQ ID NO:1.

Serial No.: 10/601,311  
Filing Date: June 20, 2003

List of References

**High-throughput protein crystallization** - RC Stevens - *Curr. Opin. Struct. Biol.*, 2000

**Overview of Protein Crystallization Methods**- PC Weber - *Methods in enzymology*, 1997

**Comparative studies of protein crystallization by vapour-diffusion and microbatch techniques** - NE Chayen - *Acta Crystallogr D Biol Crystallogr*, 1998

**An approach to rapid protein crystallization using nanodroplets** - DC Uber, EW Cornell, RA Nordmeyer, WF Kolbe, J Jin - *J Appl Crystallogr*, 2002

**An automated system for micro-batch protein crystallization and screening** - NE Chayen, PD Shaw Stewart, DL Maeder, DM Blow - *Journal of Applied Crystallography*, 1990

**Protein crystallization for genomics: towards high-throughput optimization techniques** - NE Chayen, E Saridakis - *Acta Crystallographica Section D Biological Crystallography*, 2002

**Protein Crystallization** - SD Durbin, G Feher - *Annual Review of Physical Chemistry*, 1996

**System for Evaluating Protein Crystallization Conditions by Microbatch and Vapor-Diffusion Methods** - B Zheng, JD Tice, LS Roach, RF Ismagilov - *Angewandte Chemie International Edition*, 2004

**Principles of Protein X-Ray Crystallography**- J Drenth - 1999

**Screening of protein crystallization conditions on a microfluidic chip using nanoliter-size droplets** - B Zheng, LS Roach, RF Ismagilov - *J Am Chem Soc*, 2003

**Protein interactions and crystallization**- DF ROSENBAUM, CF ZUKOSKI - *Journal of crystal growth*, 1996.

**Protein Crystallization: Micro Techniques Involving Vapor Diffusion**- DR Davies, DM Segal - *Methods Enzymol*, 1971

Therefore, the disclosure, taken in view of the level of skill in the art, enables a skilled artisan to practice the claimed invention without undue experimentation. As such, the rejection based on lacking of enablement is improper and should be withdrawn.

Serial No.: 10/601,311  
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CONCLUSION

AUG 07 2007

Applicants respectfully submit that the claims are now in condition for allowance and early notification to that effect is respectfully requested. If the Examiner feels there are further unresolved issues, the Examiner is respectfully requested to phone the undersigned at (415) 442-1000.

Respectfully submitted,  
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